Olfactory Receptor Cell-Based Odorant Detection

Elisabeth Smela[1], Pamela Abshire[2]

1 Department of Mechanical Engineering, University of Maryland, College Park MD
2 Dept. of Electrical & Computer Engineering, Univ. of Maryland, College Park MD

group members: Marc Dandin, Timir Datta, Im Deok Jung, Nicole Nelson, Menake Piyasena, Anshu Sarje

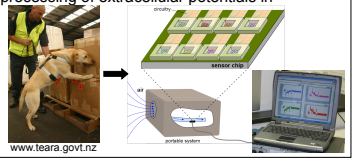
ISR @25 — The Institute for Systems Research — A. James Clark School of Engineering

Introduction

We are developing a standalone system for odorant detection and identification utilizing cell based biological sensing. A hybrid system has been designed consisting of olfactory sensory neurons integrated with proprietary CMOS IC technology for amplification and processing of extracellular potentials in response to olfactory stimuli.

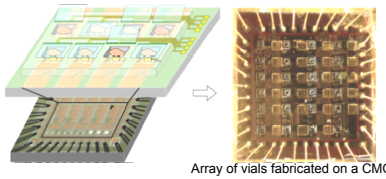
Applications include:

- Explosives detection
- Interdiction of illegal drugs
- Medical diagnosis
- Food spoilage

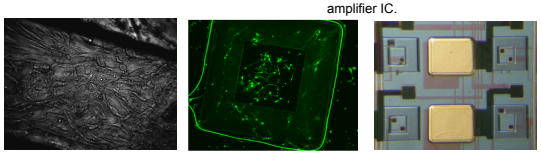


Olfactory Neurons on CMOS Surfaces

- Monitor electrical activity of olfactory sensory neurons (OSNs)
- Correlate activity across multiple, distinct OSNs
- System needs to:
  - Provide stimulus through microfluidic system
  - Measure output of multiple OSN populations simultaneously
  - Ensure cell viability by providing food and removing waste



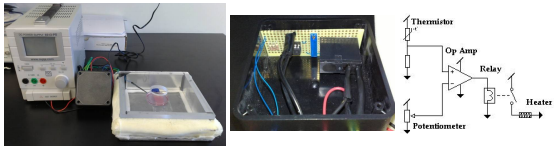
Array of vials fabricated on a CMOS amplifier IC.



OSNs inside SU8 microvial | OSNs in vial stained w/ NST | Overview of vial structures

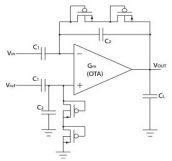
Thermal Control for Cell Viability

- Need to monitor cells over period of a few days
- Time lapse photography used to monitor cells

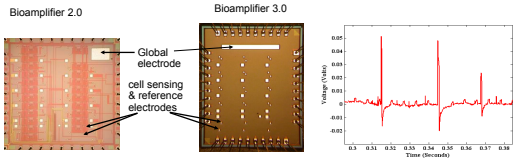


Active Arrays

Bioamplifiers in Standard CMOS

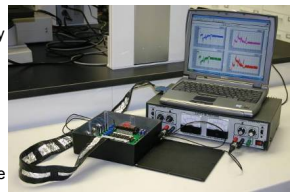


- Amplifies weak extracellular potentials originating from electrically active cells
- Bioamplifier 2.0: designed and fabricated in commercially available 0.5μm CMOS process, 6x4 array, Power Supply = +/-1.5 V, Gain = 100, Bandwidth = 3 kHz, Input Referred Noise = 25μV
- Bioamplifier 3.0: designed and fabricated in 130 nm, 8-metal ,1-poly, CMOS process. 5x3 array. Power supply =±1.25V, Gain = 40 dB, Bandwidth = 3 kHz, Input referred noise ~ 50 μV



Experimental Setup

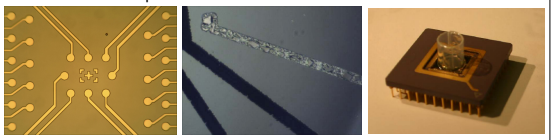
- Test board placed inside a Faraday cage for noise immunity and protection of electronic components from incubator humidity
- Cells loaded on top of the chip using standard aseptic techniques
- Test fixture maintained inside the incubator at 37 °C, 5% CO_2



Passive Arrays

Microelectrode Arrays

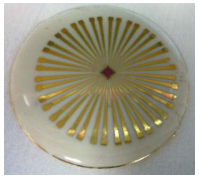
- Electrodes are Au/Ti, long traces are passivated
- Array is packaged in pin grid array ceramic package
- Au/Ti electrodes have high impedance
- Pt-black electroplated on Pt for robust electrode surface

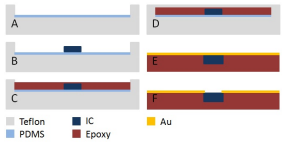


Electrode surface close-up | Pt and Pt-black electroplating | Array with vial in PGA package

Packaging

Packaging

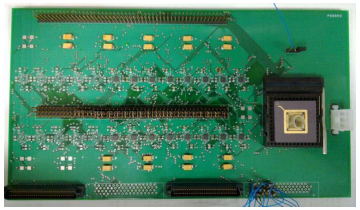




CMOS IC embedded in epoxy substrate. Two dimensional metal traces allow for a flat surface to facilitate microfluidics integration. Traces are encapsulated with SU-8 for biocompatibility. Traditional bondwires were determined to be too delicate and incompatible with fluid environment.

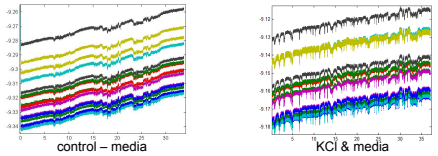
Long Term Monitoring

Electrical Hardware



- Custom PCB for extracellular potential recording
- 52 channel recording capability
- Single ended and differential amplification modes
- Low noise, high performance amplifiers
- Integration with popular commercial software platforms

Electrically Active Cell Response to KCl Stimulation



control – media | KCl & media

- KCl used to stimulate bovine smooth muscle cells
- Recordings show electrical signals vs. time for cells in media, without and with KCl

Intellectual Merit
New paradigm for odorant sensing.

Broader Impact
Benefits to society: health, safety, medicine, commerce. Interdisciplinary education.

Acknowledgements
NSF Awards CMMI0731090 and IIS0813773. Maryland NanoCenter. Prof. G. Ronnette, JHU.